

**Amendments to the Claims**

This listing of claims replaces all prior versions, and listings, of claims in the above-identified application:

**Listing of Claims**

Claims 1-57 (Previously Cancelled)

Claims 58-107 (Cancelled Herein)

108. (New) An immunostimulatory composition suitable for administration to a human subject in need of immunotherapy comprising:

(i) at least one Toll-Like Receptor (TLR) agonist which is selected from the group consisting of TLR1, TLR2, TLR3, TLR4, TLR5, TLR6, TLR7, and TLR8 agonists; and

(ii) at least one CD40 agonist that directly binds CD40; and

(iii) a pharmaceutically acceptable carrier,

wherein (i) and (ii) are each comprised in an amount such that, in combination with the other, is effective to produce a synergistic increase in a human subject in an immune response to an antigen upon administration to a human subject in need of immunotherapy.

109. (New) An immunostimulatory composition suitable for administration to a human subject in need of immunotherapy comprising:

(i) at least one Toll-Like Receptor (TLR) agonist;

(ii) at least one 4-1BB agonist that directly binds 4-1BB; and

(iii) a pharmaceutically acceptable carrier,

wherein (i) and (ii) are each comprised in an amount such that, in combination with the other, is effective to produce a synergistic increase in a human subject in an immune response to an antigen upon administration to a human subject in need of immunotherapy.

110. (New) The immunostimulatory composition of claim 109 wherein the at least one Toll-Like Receptor (TLR) agonist is selected from the group consisting of TLR1, TLR2, TLR3, TLR4, TLR5, TLR6, TLR7, TLR8 and TLR9 agonists.

111. (New) The immunostimulatory composition of claim 108 wherein the at least one CD40 agonist comprises an agonistic anti-CD40 antibody or an agonistic anti-CD40 antibody fragment.

112. (New) The immunostimulatory composition of claim 108 wherein the (ii) at least one CD40 agonist comprises a CD40 ligand (CD40L) polypeptide or a CD40L polypeptide fragment.

113. (New) The immunostimulatory composition of claim 109 wherein the (ii) at least one 4-1BB agonist comprises an anti-4-1BB antibody or an anti-4-1BB antibody fragment.

114. (New) The immunostimulatory composition of claim 109 wherein the at least one 4-1BB agonist comprises a 4-1BB ligand polypeptide or a 4-1BB ligand polypeptide fragment.

115. (New) The immunostimulatory composition of claim 108 wherein the at least one TLR agonist comprises an immune response modifier (IRM) compound or an agonist of TLR2.

116. (New) The immunostimulatory composition of claim 109 wherein the at least one TLR agonist comprises an immune response modifier (IRM) compound or an agonist of TLR2.

117. (New) The immunostimulatory composition of claim 108 wherein the at least one TLR agonist comprises an IRM compound, MALP-2, Pam3cys, LPS, polyIC or a combination of the foregoing.

118. (New) The immunostimulatory composition of claim 109 wherein the at least one TLR agonist comprises an IRM compound, MALP-2, Pam3cys, LPS, polyIC, CPG or a combination of the foregoing.

119. (New) The immunostimulatory composition of claim 108 wherein the at least one TLR agonist comprises an imidazoquinoline amine, a tetrahydroimidazoquinoline amine, an imidazopyridine amine, a 1,2-bridged imidazoquinoline amine, a 6,7-fused cycloalkylimidazopyridine amine, an imidazonaphthyridine amine, a tetrahydroimidazonaphthyridine amine, an oxazoloquinoline amine, a thiazoloquinoline amine, an oxazolopyridine amine, a thiazolopyridine amine, an oxazolonaphthyridine amine, or a thiazolonaphthyridine amine.

120. (New) The immunostimulatory composition of claim 109 wherein the at least one TLR agonist comprises an imidazoquinoline amine, a tetrahydroimidazoquinoline amine, an imidazopyridine amine, a 1,2-bridged imidazoquinoline amine, a 6,7-fused cycloalkylimidazopyridine amine, an imidazonaphthyridine amine, a tetrahydroimidazonaphthyridine amine, an oxazoloquinoline amine, a thiazoloquinoline amine, an oxazolopyridine amine, a thiazolopyridine amine, an oxazolonaphthyridine amine, or a thiazolonaphthyridine amine.

121. (New) The immunostimulatory composition of claim 108 wherein the at least one CD40 agonist comprises an anti-CD40 agonistic antibody.

122. (New) The immunostimulatory composition of claim 108 which is suitable for administration to a human subject in need of immunotherapy by a route selected from the group consisting of oral, nasal, topical, and injection.

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123. (New) The immunostimulatory composition of claim 109 which is suitable for administration to a human subject in need of immunotherapy by a route selected from the group consisting of oral, nasal, topical, and injection.

124. (New) The immunostimulatory composition of claim 108 which is suitable for injection to a human subject in need of immunotherapy.

125. (New) The immunostimulatory composition of claim 109 which is suitable for injection to a human subject in need of immunotherapy.

126. (New) The immunostimulatory composition of claim 122 wherein injection is selected from the group consisting of subcutaneous, intravenous, intraperitoneal, intramuscular and intravenous.

127. (New) The immunostimulatory composition of claim 123 wherein injection is selected from the group consisting of subcutaneous, intravenous, intraperitoneal, intramuscular and intravenous.

128. (New) The immunostimulatory composition of claim 109 wherein the at least one TLR agonist is a TLR9 agonist.

129. (New) The immunostimulatory composition of claim 128 wherein the TLR agonist comprises a CpG compound.

130. (New) A vaccine composition suitable for administration to a human subject in need thereof comprising:

(i) at least one TLR agonist which is selected from the group consisting of TLR1, TLR2, TLR3, TLR4, TLR5, TLR6, TLR7, and TLR8 agonists;

(ii) at least one CD40 agonist that directly binds CD40;

(iii) at least one antigen; and

(iv) at least one pharmaceutically acceptable carrier;

wherein (i) and (ii) are each comprised in an amount that, in combination with the other, is effective for inducing a synergistic immune response to the (iii) antigen in a human subject upon administration of the vaccine.

131. (New) A vaccine composition suitable for administration to a human subject in need thereof comprising:

(i) at least one TLR agonist;

(ii) at least one 4-1BB agonist that directly binds 4-1BB;

(iii) at least one antigen; and

(iv) at least one pharmaceutically acceptable carrier;

wherein (i) and (ii) are each comprised in an amount that, in combination with the other, is effective for inducing a synergistic immune response to the (iii) antigen in a human subject upon administration of the vaccine.

132. (New) The vaccine composition of claim 131 wherein the (i) at least one TLR agonist is selected from the group consisting of TLR1, TLR2, TLR3, TLR4, TLR5, TLR6, TLR7, TLR8 and TLR9 agonists.

133. (New) The vaccine composition of claim 130 wherein the at least one CD40 agonist comprises an agonistic anti-CD40 antibody or an agonistic anti-CD40 antibody fragment.

134. (New) The vaccine composition of claim 130 wherein the (ii) at least one CD40 agonist comprises a CD40 ligand (CD40L) polypeptide or a CD40L polypeptide fragment.

135. (New) The immunostimulatory composition of claim 131 wherein the (ii) at least one 4-1BB agonist comprises an agonistic anti-4-1BB antibody or an agonistic anti-4-1BB antibody fragment.

136. (New) The immunostimulatory composition of claim 131 wherein the at least one 4-1BB agonist comprises a 4-1BB ligand polypeptide or a 4-1BB ligand polypeptide fragment.

137. (New) The vaccine composition of claim 130 wherein the at least one TLR agonist comprises an immune response modifier (IRM) compound or an agonist of TLR2.

138. (New) The vaccine composition of claim 131 wherein the at least one TLR agonist comprises an immune response modifier (IRM) compound or an agonist of TLR2.

139. (New) The vaccine composition of claim 130 wherein the TLR agonist comprises an IRM compound, MALP-2, Pam3cys, LPS, polyIC, or a combination of the foregoing.

140. (New) The vaccine composition of claim 131 wherein the TLR agonist comprises an IRM compound, MALP-2, Pam3cys, LPS, polyIC, CpG or a combination of the foregoing.

141. (New) The vaccine composition of claim 130 wherein the TLR agonist comprises an imidazoquinoline amine, a tetrahydroimidazoquinoline amine, an imidazopyridine amine, a 1,2-bridged imidazoquinoline amine, a 6,7-fused cycloalkylimidazopyridine amine, an

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imidazonaphthyridine amine, a tetrahydroimidazonaphthyridine amine, an oxazoloquinoline amine, a thiazoloquinoline amine, an oxazolopyridine amine, a thiazolopyridine amine, an oxazolonaphthyridine amine, or a thiazolonaphthyridine amine.

142. (New) The vaccine composition of claim 131 wherein the TLR agonist comprises an imidazoquinoline amine, a tetrahydroimidazoquinoline amine, an imidazopyridine amine, a 1,2-bridged imidazoquinoline amine, a 6,7-fused cycloalkylimidazopyridine amine, an imidazonaphthyridine amine, a tetrahydroimidazonaphthyridine amine, an oxazoloquinoline amine, a thiazoloquinoline amine, an oxazolopyridine amine, a thiazolopyridine amine, an oxazolonaphthyridine amine, or a thiazolonaphthyridine amine.

143. (New) The vaccine composition of claim 130 wherein the at least one CD40 agonist comprises an anti-CD40 agonistic antibody.

144. (New) The vaccine composition of claim 130 which is suitable for administration to a human subject in need of immunotherapy by a route selected from the group consisting of oral, nasal, topical, and injection.

145. (New) The vaccine composition of claim 131 which is suitable for administration to a human subject in need of immunotherapy by a route selected from the group consisting of oral, nasal, topical, and injection.

146. (New) The vaccine composition of claim 144 which is suitable for injection to a human subject in need of immunotherapy.

147. (New) The vaccine composition of claim 145 which is suitable for injection to a human subject in need of immunotherapy.

148. (New) The vaccine composition of claim 146 wherein injection is selected from the group consisting of subcutaneous, intravenous, intraperitoneal, intramuscular and intravenous.

149. (New) The vaccine composition of claim 147 wherein injection is selected from the group consisting of subcutaneous, intravenous, intraperitoneal, intramuscular and intravenous

150. (New) The vaccine composition of claim 131 wherein the at least one TLR agonist comprises a TLR9 agonist.

151. (New) The vaccine composition of claim 150 wherein the at least one TLR9 agonist comprises a CpG compound.

152. (New) The vaccine composition of claim 130 wherein the at least one TLR agonist comprises an agonist of TLR7 or TLR8.

153. (New) The vaccine composition of claim 131 wherein the at least one TLR agonist comprises an agonist of TLR7, TLR8 or TLR9.

154. (New) The vaccine composition of claim 130 wherein the at least one TLR agonist comprises an agonist of TLR8.

155. (New) The vaccine composition of claim 131 wherein the at least one TLR agonist comprises an agonist of TLR8.

156. (New) The vaccine composition of claim 130 wherein the at least one TLR agonist comprises an agonist of TLR7.

157. (New) The vaccine composition of claim 131 wherein the at least one TLR agonist comprises an agonist of TLR7.

158. (New) A method of human immunotherapy which comprises administering to a human subject in need thereof an immunostimulatory composition according to claim 108 under conditions that elicit a synergistic effect on an immune response to an antigen.

159. (New) A method of human immunotherapy which comprises administering to a human subject in need thereof an immunostimulatory composition according to claim 109 under conditions that elicit a synergistic effect on an immune response to an antigen.

160. (New) The method of claim 158 wherein the immunostimulatory composition is administered via injection.

161. (New) The method of claim 159 wherein the immunostimulatory composition is administered via injection.

162. (New) The method of claim 160 wherein injection is selected from the group consisting of intraperitoneal, intramuscular, intravenous, and subcutaneous.

163. (New) The method of claim 161 wherein injection is selected from the group consisting of intraperitoneal, intramuscular, intravenous, and subcutaneous.

164. (New) The method of claim 158 wherein the administered immunostimulatory composition comprises a CD40 agonistic antibody or agonistic anti-CD40 antibody fragment.

165. (New) The method of claim 158 wherein the administered immunostimulatory composition comprises an agonistic CD40L polypeptide or an agonistic CD40L polypeptide fragment.

166. (New) The method of claim 159 wherein the at least one TLR agonist comprised in the administered immunostimulatory composition is selected from the group consisting of a TLR1, TLR2, TLR3, TLR4, TLR5, TLR6, TLR7, TLR8, and a TLR9 agonist.

167. (New) The method of claim 158 wherein the administered immunostimulatory composition comprises at least one TLR7 or TLR8 agonist.

168. (New) The method of claim 159 wherein the administered immunostimulatory composition comprises at least one TLR7, TLR8 or TLR9 agonist.

169. (New) The method of claim 160 wherein the administered immunostimulatory composition comprises an agonistic an anti-4-1BB antibody or an agonistic anti-4-1BB antibody fragment or a 4-1BB ligand polypeptide.

170. (New) A method of immunotherapy which comprises administering to a human subject in need thereof a vaccine composition according to claim 130 under conditions that elicit a synergistic increase in an immune response to an antigen.

171. (New) A method of immunotherapy which comprises administering to a human subject in need thereof a vaccine composition according to claim 131 under conditions that elicit a synergistic increase in an immune response to an antigen.

172. (New) The method of claim 170 wherein the vaccine composition is administered via an injection route.

173. (New) The method of claim 171 wherein the vaccine composition is administered via an injection route.

174. (New) The method of claim 172 wherein injection route is selected from the group consisting of intraperitoneal, intramuscular, intravenous, and subcutaneous.

175. (New) The method of claim 173 wherein injection route is selected from the group consisting of intraperitoneal, intramuscular, intravenous, and subcutaneous.

176. (New) The method of claim 170 wherein the administered vaccine composition comprises a CD40 agonistic antibody or agonistic anti-CD40 antibody fragment.

177. (New) The method of claim 170 wherein the vaccine composition comprises a CD40L polypeptide or a CD40L polypeptide fragment.

178. (New) The method of claim 171 wherein the administered vaccine comprises a TLR agonist selected from the group consisting of a TLR1, TLR2, TLR3, TLR4, TLR5, TLR6, TLR7, TLR8 and TLR9 agonist.

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179. (New) The method of claim 170 wherein the administered vaccine comprises a TLR7 or TLR8 agonist.

180. (New) The method of claim 171 wherein the administered vaccine comprises a TLR7, TLR8 or TLR9 agonist.

181. (New) The method of claim 171 wherein the administered vaccine comprises a TLR9 agonist .

182. (New) The method of claim 171 wherein the administered vaccine comprises an anti-4-1BB agonistic antibody. or an agonistic anti-4-1BB antibody fragment.

183. (New) The method of claim 170 wherein the administered vaccine comprises a tumor antigen, a viral antigen, a bacterial antigen, or a parasitic antigen.

184. (New) The method of claim 171 wherein the administered vaccine comprises a tumor antigen, a viral antigen, a bacterial antigen, or a parasitic antigen.